A New Avenue Opens for Treating KS, CMV and Other Herpes Diseases

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Researchers have discovered several drugs with the potential for treating a number of diseases caused by herpes viruses, including Kaposi's sarcoma (KS)and cytomegalovirus (CMV), according to study a published online in *Nature Chemical Biology*. These findings, publicized by the University of California at San Francisco (UCSF), may offer hope for people with these diseases who have not responded to available medications or for whom current treatments are too toxic.

HIV has been unique in the world of viral infections. Though its discovery is fairly recent, about two dozen medications are approved to treat it—many more drugs than those available to treat other viral infections, including those that have been known about longer than HIV.

The family of herpes viruses has been a much tougher nut to crack. Specifically, researchers have hoped to duplicate the success they had with protease inhibitors in HIV. These drugs bind to the inside of HIV's donut shaped protease enzyme, thus preventing the virus from making infectious copies of itself. Scientists, however, have experienced great difficulty discovering compounds that can effectively latch on to mature herpes protease enzymes, thus drug development has been stymied.

Hoping to buck that problem, Tina Shahian, PhD, Charles Craik, PhD, and their colleagues from UCSF started looking at the herpes virus protease enzyme at an earlier unstable phase of its development. Through laboratory experiments, they found sites on the immature protease that prevented the two ends of the enzyme from forming its necessary donut shape, thus rendering it ineffective.

After screening several dozen drugs that disrupt the development of new protease enzymes, they found several that were quite potent against Kaposi's sarcoma–associated herpesvirus (KSHV) and CMV. "All known herpes virus proteases are structurally similar," Craik said. "The inhibitor we found knocks out not only KS, but also the cytomegalovirus protease, so the site we've identified here could be a target for a broad-acting inhibitor against the entire viral family."

Though the drugs they found aren't at all ready for human testing, the work of Shahian, Craik and their colleagues could pave the way for drug development that could substantially move the treatment of all herpes viruses a huge leap forward.